

Pituitary Apoplexy: Diagnosis and Management

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Learning Objectives: After reading this article, the participant should be able to:

1. Identify the clinical manifestations of pituitary apoplexy.
2. Describe the radiographic characteristics of pituitary apoplexy.
3. Recall the importance of rapid diagnosis and treatment of pituitary apoplexy.

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Pituitary apoplexy, an uncommon complication of pituitary adenomas, was first described in 1898 when Pearce Bailey reported hemorrhage into a pituitary adenoma in a 50-year-old man with acromegaly. The patient presented with sudden onset of headache, nausea, vomiting, fever, oculomotor palsies, and visual loss. Postmortem examination revealed hemorrhage in the intrasellar adenoma and endarteritis of the adenohypophyseal vasculature. A similar case was reported in 1905 of a 21-year-old man with acromegaly who presented with acute hemorrhage and necrosis into a pituitary adenoma. This clinical entity remained somewhat obscure until 1950, when Brougham and co-workers reported postmortem findings of acute degenerative changes in pituitary adenomas in five cases. They described a clinicopathological syndrome characterized by an abrupt onset of headache, ophthalmoplegia, blindness, stupor, or coma, and named it *pituitary apoplexy*. It is postulated that this condition is caused by sudden expansion of a pituitary adenoma secondary to hemorrhage into or infarction of the tumor mass, which leads to compression of local suprasellar and parasellar structures.

Various definitions have been proposed for pituitary apoplexy. Although patients with pituitary tumors may have clinically silent hemorrhages, the term *pituitary apoplexy* should be reserved for the clinical syndrome of an apoplectic event

characterized by a sudden onset of headache associated with neurologic or endocrinologic abnormalities attributed to a massive hemorrhage or infarction in a pituitary tumor. The syndrome often occurs in patients with no antecedent history suggestive of a pituitary tumor, and it may be the first definite indication that a pituitary tumor is present.

Incidence

The mean age of patients with pituitary apoplexy is approximately 45 years, with a slight male predominance. Cyst formation, regions of hemorrhage, and necrosis are commonly found in pituitary adenomas at autopsy and are not necessarily associated with clinical pituitary apoplexy. Hemorrhage in a pituitary tumor that is not associated with a clinical apoplectic event has been seen in up to 25% of pituitary tumors. The incidence of pituitary tumors is between 2.7% and 22.5% at autopsy.

Clinical Presentation

Apoplectic hemorrhage or infarction in a pituitary adenoma causes the lesion to enlarge, leading to acute compression of the sellar and parasellar structures. Clinical signs and symptoms include sudden onset of headache, nausea, vomiting, diplopia, and visual impairment. Headache, the most common symptom, often is described as excruciating and sudden in onset, and often is accompanied by nausea and vomiting. Suprasellar tumor expansion leads to compression of the visual apparatus, which may produce precipitous

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Category: Tumor

Key Words: Pituitary adenoma, Pituitary apoplexy, Transphenoidal surgery

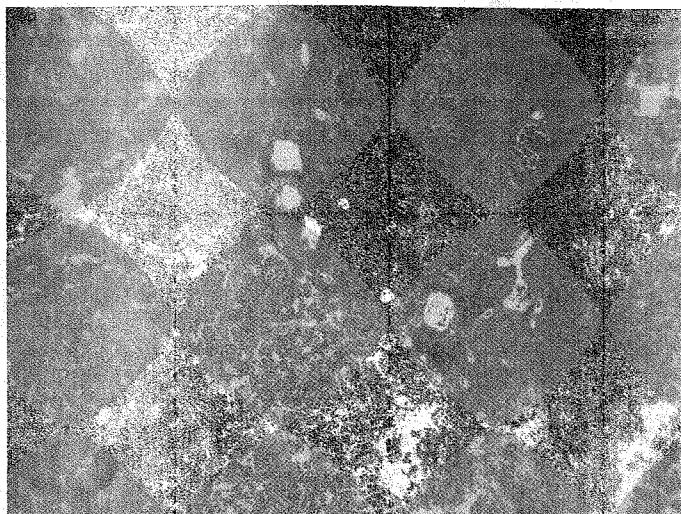


Figure 1. Photomicrograph of a hemorrhagic and necrotic non-functioning pituitary adenoma in a patient with pituitary apoplexy (hematoxylin and eosin; original magnification, $\times 100$).

deterioration of visual acuity or reduction in fields, leading to blindness. The classic visual field deficit is a bitemporal superior quadrantanopia from compression of the inferior aspect of the optic chiasm. Less commonly, the optic tract can be compressed in a prefixed chiasm, resulting in a homonymous hemianopsia. Conversely, compression of the optic nerve in a postfixed chiasm can produce central scotoma, monocular visual acuity, and pain on eye movement, often mimicking optic neuritis. Hypothalamic involvement also may produce hypotension, disturbances of temperature regulation, cardiorespiratory dysrhythmias, and diabetes insipidus. Lateral expansion with pressure on one or both of the cavernous sinuses results in venous stasis, internal carotid artery compression, trigeminal nerve dysfunction, and ophthalmoplegia due to compression of the oculomotor, trochlear, and abducens nerves. The oculomotor nerve is more frequently involved than the abducens nerve. Involvement of the sympathetic fibers within the cavernous sinus may produce a form of Horner's syndrome that includes unilateral ptosis, miosis, and anhidrosis limited to the forehead.

The initial neurologic deficit caused by most pituitary tumors is that of optic apparatus compression from suprasellar expansion and, much less commonly, extraocular muscle paresis from lateral compression of the cavernous sinus. By contrast, in instances of pituitary apoplexy, extraocular muscle palsies occur more often (78%) than do visual pathway deficits (52%–64%). The discrepancy may be explained by the size and competency of the diaphragma sella, but this theory has not been definitely proven.

When an acute hemorrhage in a pituitary tumor breaks through the arachnoid membrane into the cerebrospinal fluid, the sudden onset of headache associated with nausea, vomiting, meningeal irritation, neck stiffness, and photophobia with or without oculomotor paresis may be confused with an aneurysmal subarachnoid hemorrhage. Pituitary apoplexy can be especially difficult to distinguish from aneurysmal subarachnoid hemorrhage when pituitary adenomas and aneurysms co-exist. The incidence of coexisting aneurysms associated with pituitary adenomas has been reported to be 7.4%. Cerebral angiography or magnetic resonance angiography (MRA) is recommended to differentiate the two conditions. Rarely, pituitary apoplexy has been complicated by vasospasm. Mechanisms that have been suggested as explanations for this occurrence include extravasation of blood into the subarachnoid space in a mechanism similar to postaneurysmal subarachnoid hemorrhage, injury to the hypothalamus, or the possible release of vasoactive substances from the pituitary tumor.

Pathogenesis and Pathophysiology

The pathogenesis of pituitary apoplexy remains controversial. Most cases occur without any identifiable predisposing factors. A wide spectrum of situations has been described in association with pituitary apoplexy, some of which may represent pure coincidence. These associations include cardiac surgery; anticoagulation; angiography; pneumoencephalography; repetitive coughing secondary to respiratory infection; closed head trauma; estrogen therapy; bromocriptine therapy; radiotherapy; diabetic ketoacidosis;

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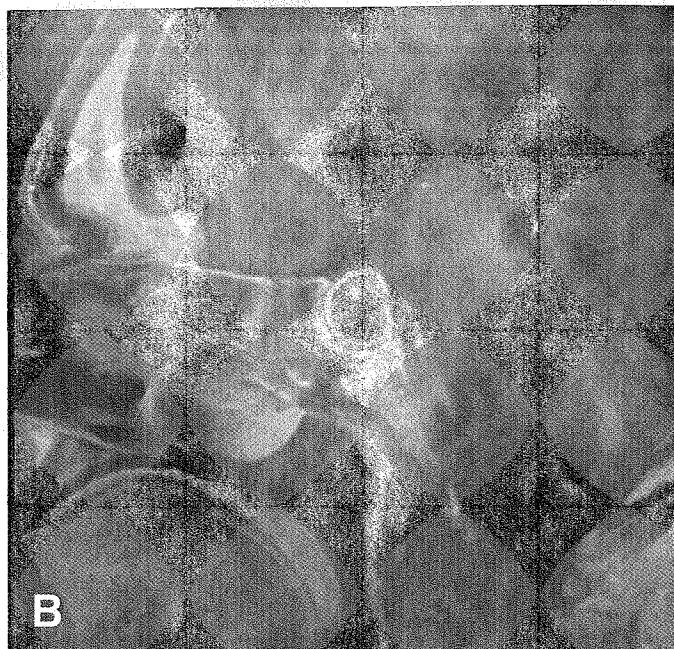
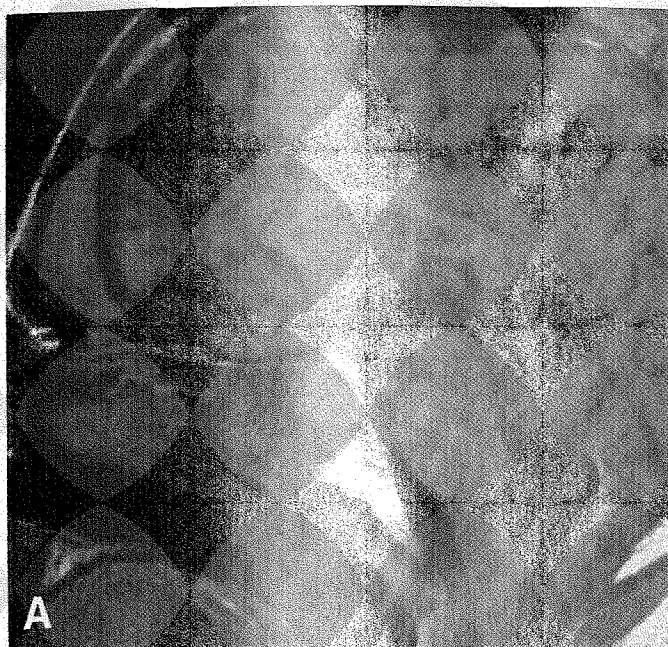


Figure 2. T1-weighted MRI scans of the brain: (A) sagittal, and (B) sagittal with gadolinium enhancement. A hemorrhagic sellar mass is seen extending superiorly, compressing the optic chiasm and inferiorly obliterating the sella. There is thickening and enhancement of the sphenoid sinus mucosa.

elevated intracranial pressure; atheromatous emboli; positive pressure mechanical ventilation; chronic antiplatelet therapy; triple bolus test (with insulin, thyrotropin-releasing hormone, and luteinizing hormone-releasing hormone); gonadotropin-releasing hormone testing; leuprolide administration for prostate cancer; dissection of the internal carotid artery; rupture of an intracavernous carotid artery aneurysm; pituitary abscess; and laparoscopic surgery.

Several interesting theories have been proposed regarding possible roles of ischemia in the pathogenesis of pituitary apoplexy. Bailey first proposed that endarteritis of the pituitary gland was the source of hemorrhage. Brougham and co-workers thought that large pituitary tumors outgrew their blood supply and developed areas of ischemic necrosis and subsequent hemorrhage. Rovit and Fein proposed that compression of the superior hypophyseal artery against the edge of the diaphragma sellae by the upward expanding tumor compromises blood flow to the gland and adenoma, leading to ischemia and necrosis. This possibility was supported by Ebersold and colleagues, who found thrombosis in the sinusoids of the tumor specimens, suggesting a mechanism of vascular stasis, ischemic necrosis, and subsequent hemorrhage.

Others, however, have refuted this theory of vascular insufficiency and compression on the basis of autopsy studies and angiographic data. Angiographic studies indicate that the blood supply to pituitary adenomas is derived primarily from the inferior hypophyseal artery, a branch from the meningohypophyseal trunk, rather than the superior hypophyseal artery. A portal vascular network is interposed between arterial and venous structures in the anterior pituitary gland. The data suggest that it is unlikely that compression of the portal system along the pituitary stalk, against the notch of the diaphragma sellae, leads to infarction and hemorrhage of the adenoma. Some authors have shown that the arterial supply of the adenoma, originat-

ing from the inferior hypophyseal artery, is under higher pressure than the sinusoids of the adenohypophysis, which may lead to spontaneous hemorrhage within the tumor. Others have



Figure 3. Unenhanced CT scan of the brain showing a hyperdense suprasellar mass without any signs of subarachnoid blood in a patient with pituitary apoplexy.

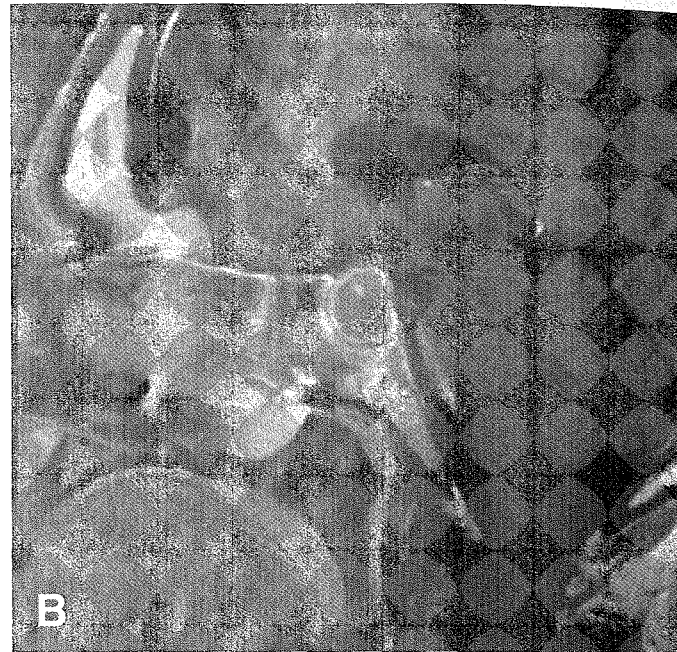
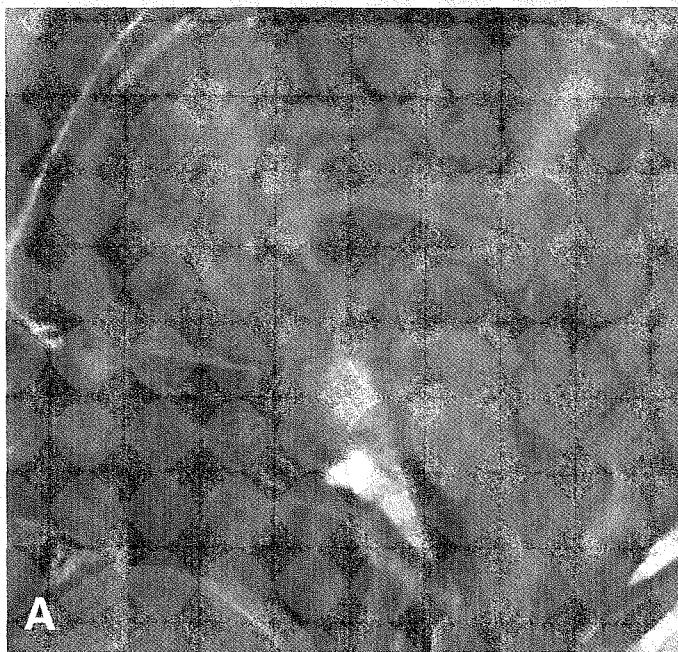


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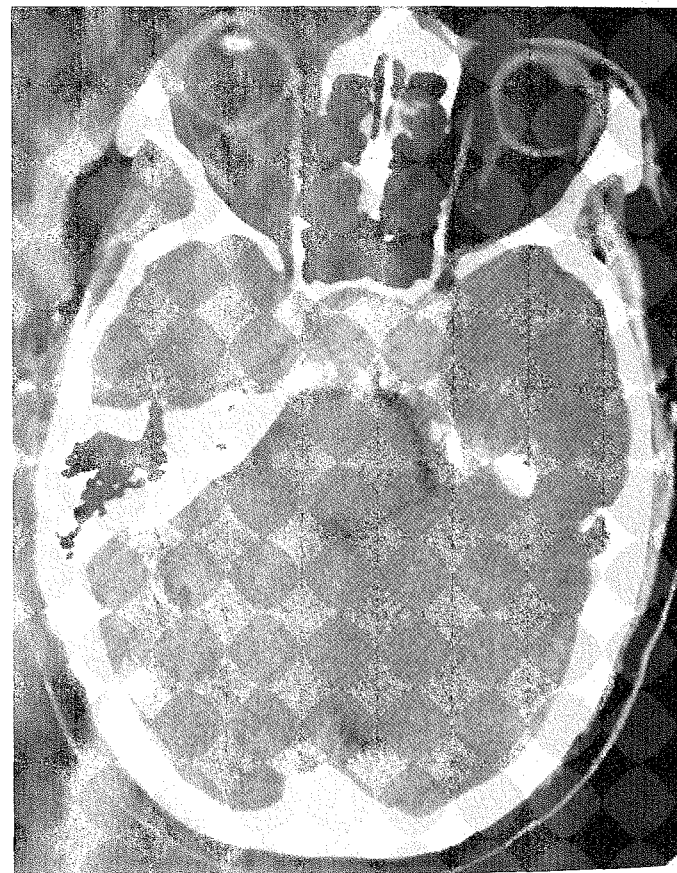


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postulated that tumor cells invade the vessel wall and disrupt the endothelial lining, leading to potential vessel rupture.

Some have suggested that the propensity for hemorrhage and infarction may be related directly to the size and vascular-

ity of the pituitary tumor. In elderly patients with diabetes, hypertension, and cardiovascular disease, atheromatous emboli may play a role in compromising blood supply to the adenoma. Sudden changes in intracranial pressure associated with pituitary apoplexy have been reported during angiography, pneumoencephalography, and laparoscopic surgery. Acute increases in intrasellar pressure and venous pressure in the cavernous sinus, which has already been occluded by lateral expansion of the

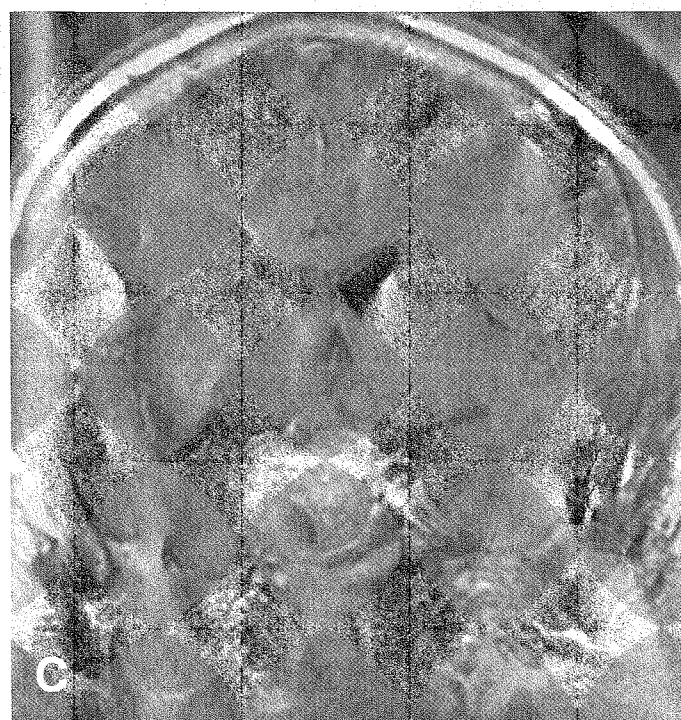
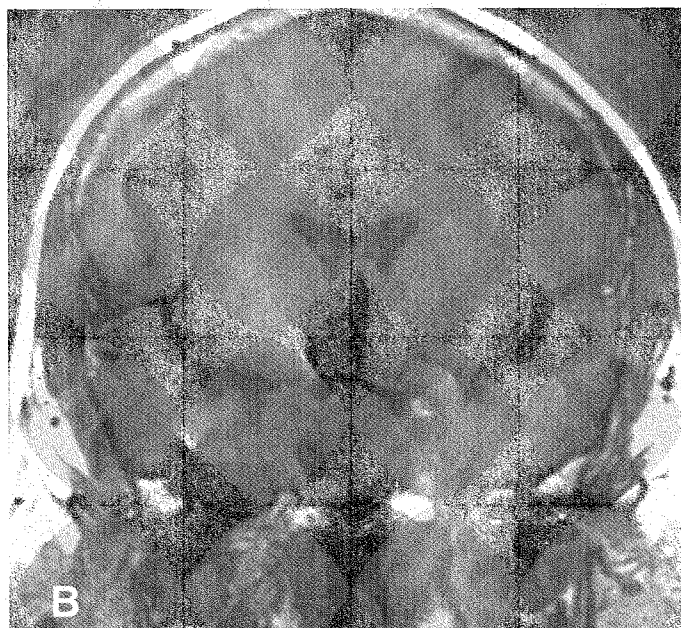
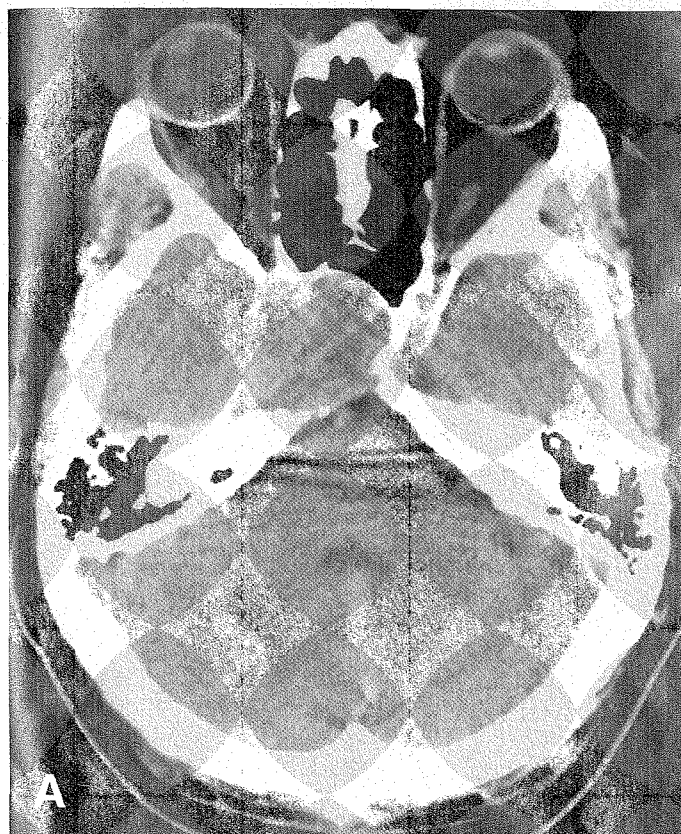


Figure 4. This patient presented with severe headache and right ophthalmoplegia secondary to nonhemorrhagic pituitary apoplexy in a macroprolactinoma. His symptoms resolved after bromocriptine therapy. **A**, Unenhanced CT scan shows a large, isodense sellar mass extending into the right cavernous sinus without evidence of hemorrhage. MRI coronal views show invasion of the right cavernous sinus and encasement of the carotid artery. **B**, T1-weighted scan. **C**, T1-weighted scan with gadolinium enhancement. **D**, T2-weighted scan. There is also thickening of the sphenoid sinus mucosa.

tumor, may impair the arterial supply to the adenoma and cause subsequent infarction, necrosis, and hemorrhage (Fig. 1).

Imaging Characteristics

Pituitary apoplexy should be suspected immediately if a patient experiences sudden onset of headache, nausea, vomiting, any change in mental status, ophthalmoplegia, or abrupt deterioration of visual acuity or fields. Failure to recognize and treat this life-threatening syndrome can lead to poor outcomes, especially if vision is compromised.

Magnetic resonance imaging is the diagnostic study of choice in imaging the sellar and parasellar region (Fig. 2). Unlike CT, MRI is nearly 100% sensitive in detecting both a tumor and an associated hemorrhage or infarct. Magnetic resonance imaging also is sensitive in detecting subacute and chronic hemorrhages within the pituitary adenoma. Macroadenomas usually appear heterogeneous because of areas of hemorrhage, infarction, or cystic formation. The parasellar dura can be thickened and enhanced on postgadolinium MRI scans. The sphenoid sinus mucosa also often is thickened during the acute stage of pituitary apoplexy (see Fig. 2). These changes are thought to be caused by venous congestion of the cavernous or circular sinus secondary to a sudden increase in intrasellar pressure.

Unenhanced CT scans may show a hyperdense signal within the adenoma if hemorrhage is present acutely (Fig. 3). Severe hemorrhages can extend into the brain parenchyma, the ventricular system, or the subarachnoid space and resemble the sequelae of a ruptured aneurysm. However, when apoplexy is caused by infarction, the tumor may be hypodense or isodense on CT scans (Fig. 4). After injection of contrast, a ring of enhancement may appear around the hypodense mass. Computed tomographic scanning with bone windows also may detect enlargement or destruction of the sella turcica, with or without sphenoid sinus opacification. Cranial radiographs, performed less commonly, may indirectly reveal pituitary abnormalities such as enlargement of the sella with undermining of the anterior clinoids, a double floor sella, and erosion of the dorsum sellae and posterior clinoids.

It is important to consider aneurysmal subarachnoid hemorrhage in the differential diagnosis, because the symptoms of acute onset headache, stiff neck, and alterations in consciousness mimic those of pituitary apoplexy. Cerebral angiography or MRA may be necessary to reach a correct diagnosis.

Management and Treatment

Initial medical management requires prompt administration of glucocorticoids because of the high prevalence of hypopituitarism and subsequent adrenal insufficiency. Glucocorticoids also may improve visual function. Endocrinologic studies should be obtained immediately. Markedly elevated levels of prolactin may suggest a prolactinoma, which may be treated with bromocriptine in the absence of visual deficits (see Fig. 4); Brisman and colleagues reported a patient with a macroprolactinoma who presented with pituitary apoplexy and a third nerve palsy that was reversed with bromocriptine and glucocorticoids. Fluid and elec-

trolyte balance should be monitored closely. Transient diabetes insipidus and, rarely, the syndrome of inappropriate secretion of antidiuretic hormone may occur secondary to involvement of the hypothalamic-pituitary axis.

Most experienced neurosurgeons advocate acute administration of glucocorticoids and emergent surgical decompression of the pituitary gland and visual apparatus via the transsphenoidal approach. This strategy is mandatory in the clinical setting of visual loss or neurologic deficits. Urgent and adequate decompression promotes significant neurologic improvement, rapid recovery of diencephalic symptoms, resolution of ocular paresis, restoration of compromised vision, and, sometimes, improvement of pituitary function.

In a retrospective analysis of 37 patients, Bills and co-workers found that those who underwent surgery within 7 days of pituitary apoplexy achieved significant recovery in visual acuity and visual field deficits. Visual improvement was retarded in patients undergoing surgery after the 7th day. Early transsphenoidal decompression resulted in improvement in ocular paresis in 100% of patients, visual acuity deficits in 88% of patients, and visual field deficits in 95% of patients. In a review by Cardoso and Peterson, the extent of visual recovery was more dependent on early transsphenoidal decompression than on the severity of the initial visual loss. Patients were more likely to recover from ocular paresis than visual loss.

Conclusion

Pituitary apoplexy is a clinical syndrome caused by hemorrhage or infarction in a pituitary adenoma. Rapid and accurate diagnosis is necessary to achieve optimal results from treatment. Magnetic resonance imaging is the diagnostic study of choice. The administration of glucocorticoids and prompt transsphenoidal surgery to decompress the optic apparatus remain the mainstay of treatment.

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1. Pituitary apoplexy is characterized by a sudden onset of headache, visual loss, and/or ophthalmoplegia secondary to hemorrhage or infarction in a pituitary tumor.

True or False?

2. Pituitary apoplexy can mimic aneurysmal subarachnoid hemorrhage if blood breaks through the arachnoid membrane.

True or False?

3. Computed tomography is the diagnostic study of choice in imaging the sellar and parasellar region.

True or False?

4. On CT scans, adenoma may appear either hyperdense, hypodense, or isodense.

True or False?

5. During the acute stage of pituitary apoplexy, MRI scans may demonstrate thickening of the sphenoid sinus mucosa.

True or False?

6. Transcranial decompression is the preferred route for surgical management of pituitary apoplexy.

True or False?

7. Immediate administration of glucocorticoids and early transsphenoidal decompression is the treatment of choice in pituitary apoplexy.

True or False?

8. Early transsphenoidal decompression provides the best chance for improvement in visual and oculomotor deficits.

True or False?

9. Some cases of apoplexy in prolactinoma have been managed with dopamine agonist therapy.

True or False?

10. In pituitary apoplexy, involvement of the parasympathetic fibers within the cavernous sinus may produce Horner's syndrome.

True or False?